

### Remarks

The June 18, 2003 Official Action and the references cited therein have been carefully considered. In view of the amendments presented herewith in these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set in the June 18, 2003 Official Action. Accordingly, the initial response period was due to expire September 18, 2003. A petition for a three (3) month extension of the response period is presented with this Amendment and Request for Reconsideration, which is being filed before the expiration of the three (3) month extension period.

In the June 18, 2003 Official Action, claim 39 is objected to because of the recitation of "channel", rather than "microchannel", and appropriate correction is required.

Turning to the substantive aspects of the June 18, 2003 Official Action, claims 40-42 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite in that claim 40 is improperly dependent. In addition, claim 40 recites that the particle is a cell, whereas claims 41 and 42, which are dependent from claim 40, call for particles other than a cell.

Claims 1, 2, 4-7, 9, 19, 24-26 and 29 have been rejected under 35 U.S.C. §102(e) as allegedly anticipated

by the disclosure of U.S. Patent 6,572,830 to Burdon et al.

Claims 1, 2, 7 and 24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by the disclosure of WO99/25816(Tai et al.).

Claims 1, 2, 4-7, 9, 11, 19, 20, 25, 26 and 29-33 have been rejected under 35 U.S.C. §102(e) as allegedly anticipated by the disclosure of U.S. patent 6,544,734 to Briscoe et al.

Claims 1-3, 11, 19-21 and 24 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable in view of WO99/38612(Cheng et al.). According to the examiner, Cheng et al discloses all of the features of claims 1-3, 11, 19-21 and 24 except that there is no express disclosure that the channels of the bioelectronic chip device described in Cheng et al. are microchannels. The examiner contends, nonetheless, that it would have been obvious for one of ordinary skill in the art at the time the present invention was made to use microchannels in the device of Cheng et al. because the flow chamber of such device has a volume of 10 $\mu$ l.

Claims 7 and 28 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable based on the combined disclosures of Briscoe et al., supra, and U.S. patent 6,322,683 to Wolk et al. The examiner contends in this regard that Briscoe et al describes the use of a pump, but fails to disclose its location, and further

that, based on the disclosure of Wolk et al., the choice of a positive pressure pump or negative pressure pump is a matter of optimization or convenience.

The foregoing objection and rejections constitute all of the grounds set forth in the June 18, 2003 Official Action for refusing the present application.

It is also indicated in the June 18<sup>th</sup> Official Action that certain claims are drawn to allowable subject matter. Specifically, claim 39 is allowed and claims 8, 10, 12-18, 22, 23, and 34-38 are indicated as allowable if rewritten in proper independent form. Claims 40-42 are also indicated as allowable if amended to overcome the above-mentioned 35 U.S.C. §112, second paragraph rejection.

In accordance with the present amendment, the subject matter of claim 2 and claim 9 (in part) has been incorporated into claim 1. Claim 1, as now amended, also calls for "exposing said at least one cell of said fluid sample to said electric field". Support for this amendatory language is provided in the present specification at page 9, lines 13-22, page 13, lines 21-25, page 19, lines 12 and 13, page 20, lines 18-21, page 25, lines 8-18 and Example I. In view of the present amendment of claim 1, claim 2 has been cancelled and a consequential amendment has been made in claim 19.

The dependencies of claims 3-5, 23 and 24 have been amended due to the cancellation of claim 2, and

further consequential amendments have been made in claims 3-5.

Independent claims 25 and 30 have been similarly amended by restating and relocating the recitation regarding "means for causing flow of a cell-containing fluid sample through said at least one microchannel", and reciting that an electric field is applied to "said flowing cell-containing fluid sample in said cell lysis region". Support for such amendment to claims 25 and 30 is provided in the present specification at page 9, lines 13-22, page 13, lines 21-25, page 19, lines 12 and 13, page 20, lines 18-21, page 25, lines 8-18 and Example I (for claim 25) and page 10 line 14 through page 11 line 1 and page 23 line 16 through page 17, line 1 (for claim 30).

Claim 39 has been amended to recite "said second microchannel" in subparagraph c thereof.

Claims 40-42 have been amended so as to be dependent from claim 39.

The present amendment also includes new claims 43 and 44, which are directed to particular embodiments of applicants' invention. Support for these new claims is provided in the present specification at page 18, lines 19-23 and page 23, lines 2-4 (for claim 43) and page 7, lines 22-24 and Example II (for claim 44). The appropriate fee for one additional dependent claim is included with this response.

No new matter has been introduced into this application by reason of any of the claim amendments presented herewith.

As a result of the foregoing amendments, the objection to claim 39 and the 35 U.S.C. §112, second paragraph rejection of claims 40-42 are believed to be overcome, and claims 39-42 are all in condition for allowance. Thus, the only matters remaining to be addressed are the various prior art rejections set forth in paragraphs 3-9 of the June 18th Official Action. These last-mentioned grounds of rejection cannot be maintained in view of the amendments presented herewith and are, therefore, respectfully traversed.

**A. Burdon et al. Fails to Anticipate the Subject Matter of**

**Claims 1, 2, 4-7, 9, 19, 24-26 and 29**

Rejections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the allegedly anticipatory prior art reference. In re Arkley, 172 USPQ 524 (CCPA1972).

Applying this rule of law to the present case, the 35 U.S.C. §102 (e) rejection of claims 1,2, 4-7, 9, 19, 24-26 and 29 based on Burdon et al. is improper because Burdon et al. fails to identically disclose or describe the subject matter of those claims.

As presently amended independent claims 1 and 25 require exposure of the flowing fluid sample to an

electric field in order to effect lysis of a cell or cells present in the sample. In this respect, the present invention is readily distinguishable from Burdon et al., which discloses a microfluidic device for performing cell lysis, wherein the cell sample is disposed in a cavity or well, with the sample remaining in the cavity for some finite residence time during which cell lysis occurs. For example, cell lysis may be carried out in cavity 572 of the device shown in Figure 17 of Burdon et al. During the cell lysis operation, the fluid sample (including cells present therein) is essentially static with no net sample flow through the system. In contradistinction to Burdon et al., the present invention utilizes a mode of operation wherein the cell-containing sample is caused to flow during cell lysis.

In summary, given that Burdon et al. fails to identically disclose or describe all of the recitations of applicants' claims 1, 2, 4-7, 9, 19, 24-26 and 29 §102(e) rejection of those claims based on Burdon et al is untenable and should be withdrawn.

**B. Tai et al. Fails to Anticipate the Subject Matter of  
Claims 1, 2, 7 and 24**

The same distinctions noted above between applicants' invention and that of Burdon et al. also serve to distinguish applicants' invention from Tai et al. The cell lysis device of Tai et al. includes barriers

(elements 120 shown in Figure 1; and 210 in Figure 2C) which function to hold the cell in place, as disclosed at page 4, lines 9-11 and lines 27-29. Thus, the cell lysis device of Tai et al. does not operate by exposing the flowing cell-containing fluid sample to an electric field in order to effect cell lysis, as required in amended claim 1.

Furthermore, as presently amended, claim 1 calls for analyzing the volume of analyte in the microchannel structure. Tai et al. plainly fails to identically disclose or describe this feature of applicants' invention.

In view of the above-noted differences between the invention disclosed in Tai et al. and the presently claimed invention, the §102(b) rejection of claims 1, 2, 7 and 24 based on Tai et al, is improper and should be withdrawn.

**c. Briscoe et al. Fails to Anticipate the Subject Matter of Claims 1, 2, 4-7, 9, 11, 19, 20, 25, 26 and 29-33**

The Briscoe et al. patent is related to the Burdon et al., supra, in that the former is a continuation-in-part of the latter.

The microfluidic system of Briscoe et al., like that of Burdon et al., is provided with a cavity or well for performing cell lysis. See, for example, cell lysis chamber 50 in Figure 3 of Briscoe et al. In this

connection Briscoe et al. discloses at column 3, lines 54-56 that "After cell lysis, fluid control system 30 allows the fluid containing the cell contents to pass to a DNA separation chamber 16. This is unquestionably a description of a batch-type process in which the sample is transferred between different cavities or chambers in sequential fashion. That being the case, the present invention is patentably distinguishable from that of Briscoe et al. for at least the same reasons discussed above in establishing the impropriety of the §102(e) rejection of claims 1, 2, 4-7, 9, 19, 24-26 and 29 based on Burdon et al. Accordingly, §102(e) rejection of claims 1,2,4-7,9, 11, 19, 20, 25, 26 and 29-33 based on Briscoe et al. should also be withdrawn as it is untenable in view of the present amendment of those claims.

**D. Cheng et al. Fails to Render Obvious the Subject Matter of Claims 1-3, 11, 19-21 and 24**

The examiner's reliance on Cheng et al. as evidence of obviousness in rejecting claims 1-3, 11, 19-21 and 24 is clearly misplaced.

Applicant respectfully takes exception to the examiner's characterization of elements 18A and 18B in Figure 1 of Cheng et al. as "channels". First of all, such a characterization is inconsistent with the description of the bioelectronic chip of Cheng et al. as "channel-less". See the title of the patent application



of Cheng et al. and page 9, line 5. More importantly, Cheng et al. describe elements 18A and 18B as "plastic tubing". See page 11, lines 4-6 of Cheng et al. Such plastic tubing is structurally distinct from the silicon chip substrate of Cheng et al. and certainly does not constitute a "substrate having a microchannel structure which includes at least one microchannel therein", as recited in claim 1.

Furthermore, cell lysis as performed using the channel-less bioelectronic chip of Cheng et al. is a static or batch-type operation, as contrasted with the dynamic cell lysis technique devised by applicants, in which a flowing, cell-containing fluid sample is exposed to an electric field in order to effect cell lysis.

In addition, there is no teaching or suggestion in Cheng et al. of "analyzing said volume in said microchannel structure beyond said cell lysis region", as called for in applicants' claims 19-21. On the contrary, post-lysis analysis in the channel-less bioelectronic chip device of Cheng et al. occurs in the same chamber as the lysis operation.

In summary, Cheng et al. describes a device whose structure and mode of operation is substantially different from that of the present invention. In view of these differences Cheng et al. cannot reasonably be regarded as rendering applicants' invention obvious. Accordingly, the §103(a) rejection of claims 1-3, 11, 19-

21 and 24 based on Cheng et al. should be withdrawn.

**E. The Combined Disclosures of Briscoe et al. and Wolk et al. Fail to Render Obvious the Subject Matter of Claims 27 and 28**

Concerning the rejection of claims 27 and 28 based on Briscoe et al. in view of Wolk et al., the examiner's position in this regard is untenable, for at least the same reasons previously discussed with respect to the impropriety of the §102(e) rejection based on Briscoe et al. Given that Wolk et al. fails to compensate for the fundamental deficiencies noted above in the disclosure of Briscoe et al., the rejection of claims 27 and 28 based on the combined disclosures of Briscoe et al. and Wolk et al. is improper and should also be withdrawn.

In view of the amendment presented herewith and the foregoing remarks, all of the claims now pending in this application are believed to be in condition for allowance.

Accordingly, the issuance of a Notice of Allowance is in order, and such action is earnestly solicited.

Respectfully submitted

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Enclosures:

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